AMENDMENTS TO THE CLAIMS

This listing of the claims replaces all prior versions of the claims in the application.

Listing of claims

1. (Currently Amended) A method of determining a likelihood of a fetus carried by a pregnant mother having a chromosomal abnormality using a first biological parameter and a second biological parameter, both of which [[~~is~~]] parameters are suitable for screening said fetus for said chromosomal abnormality, the method comprising:

receiving first data from a first stage of pregnancy of said mother, said first data comprising data representing a first value of said first biological parameter which is PAPP-A ~~, said first biological parameter comprising one of total hCG, PAPP-A, Inhibin-A, AFP, and uE$_3$~~, and data representing a first value of [[~~a~~]] said second biological parameter, said second biological parameter comprising one of total hCG, ~~PAPP-A,~~ Inhibin-A, AFP, and uE$_3$~~, wherein said second biological parameter is suitable for screening said fetus for said chromosomal abnormality~~;

receiving second data from a second, later stage of said pregnancy, said second data comprising data representing a second value of said first biological parameter and data representing a second value of said second biological parameter;

wherein said first biological parameter is a marker for said chromosomal abnormality at the first stage of pregnancy and has substantially no value as a marker during the second stage of pregnancy, and

wherein said second biological parameter is a marker for said chromosomal abnormality at said second stage of pregnancy and has substantially no value as a marker during the first stage of pregnancy,

determining, using a computer, a multiple of median value for each of said values in said first and second data by dividing each of said values in said first and second data by a corresponding predicted median value;

forming, using a computer, a feature vector y using said multiple of median values;

determining a probability of an unaffected pregnancy given feature vector y;

determining a probability of an affected pregnancy given feature vector y, and

determining likelihood ratio data from said first and second data by calculating, using a computer, a ratio of said probability of an unaffected pregnancy to said probability of an affected pregnancy, said likelihood ratio data representing the likelihood of said fetus having a chromosomal abnormality.

2. (Cancelled)

3. (Original) A method as claimed in claim 1 wherein said first biological parameter has a logarithm multiple of median (log MoM) value closer than one standard deviation to zero.

4. (Previously presented) A method as claimed in claim 1, wherein in a cohort of pregnancies having said abnormality said first biological parameter is selected such that a correlation coefficient of said first and second values of said parameter is greater than 0.3.

5. (Cancelled)

6. (Cancelled)

7. (Cancelled)

8. (Cancelled)

9. (Previously presented) A method as claimed in claim 1 wherein in a cohort of pregnancies having said abnormality said second biological parameter is selected such that a correlation coefficient of said first and second values of said parameter is greater than 0.3.

10. (Cancelled)

11. (Cancelled)

12. (Previously presented) A method as claimed in claim 1 wherein said first data further comprises data obtained from an ultrasound scan performed on said mother.

13. (Cancelled)

14. (Previously presented) A method as claimed in claim 1 further comprising adjusting said first and second data responsible to one or more covariates prior to determining said likelihood ratio.

15. (Previously presented) A method as claimed in claim 1 further comprising adjusting said likelihood ratio by a prior probability factor dependent upon an age of said mother.

16. (Previously presented) A method as claimed in claim 1 wherein said first stage of pregnancy comprises a first trimester of said pregnancy and said second stage of said pregnancy comprises a second trimester of said pregnancy.

17. (Previously presented) A method as claimed in claim 1 wherein said first stage of pregnancy comprises a stage of said pregnancy from 8 to 13 weeks, and wherein said second stage of said pregnancy comprises a stage of said pregnancy from 14 to 22 weeks.

18. (Previously presented) A method as claimed in claim 1 wherein said fetus is a human fetus.

19. (Previously presented) A method as claimed in claim 1 wherein said chromosomal abnormality comprises Down's Syndrome.

20. (Currently amended) A method of determining whether a pregnant woman is at an increased risk of having a fetus with Down's Syndrome, the method comprising the steps of:

measuring a first screening marker level from ~~one of~~ a first ~~and second~~ stage of pregnancy by assaying a sample obtained from the pregnant woman at said first ~~or second~~ stage of pregnancy for ~~at least one~~ a first biochemical screening marker, ~~said~~ which first screening marker is PAPP-A; ~~comprising one of total hCG, PAPP-A, Inhibin-A, AFP, and uE$_3$;~~;

measuring a level of the same said first screening marker at ~~the other of said first and~~ a second stage of pregnancy by assaying a sample obtained from the pregnant woman

at said ~~other~~ second stage of pregnancy for said at least one biochemical screening marker;

measuring a second screening marker level from ~~one of~~ said first ~~and second~~ stage of pregnancy by assaying a sample obtained from the pregnant woman at said first ~~or second~~ stage of pregnancy for said second biochemical screening marker, said second screening marker comprising one of total hCG, ~~PAPP-A,~~ Inhibin-A, AFP, and uE_3;

measuring a level of said second screening marker at ~~the other of said first and~~ said second stage of pregnancy by assaying a sample obtained from the pregnant woman at said ~~other~~ second stage of pregnancy for said second biochemical screening marker;

wherein said first biochemical screening marker is a marker for said chromosomal abnormality at the first stage of pregnancy and has substantially no value as a marker during the second stage of pregnancy, and

wherein said second biochemical screening marker is a marker for said chromosomal abnormality at said second stage of pregnancy and has substantially no value as a marker during the first stage of pregnancy,

determining, using a computer, a quantitative estimate of the risk of Down's Syndrome using the measured screening marker levels from both the first and second stages of pregnancy by expressing each of said measured screening marker levels as a logarithm of a multiple median value by dividing each of said measured screening marker levels by a corresponding predicted median value to form a feature vector y; and

determining said quantitative estimate from a ratio of a probability of an unaffected pregnancy given feature vector y and a probability of an affected pregnancy in which said fetus has said abnormality given feature vector y.

21. (Cancelled)

22. (Cancelled)

23. (Previously presented) A method as claimed in claim 20 wherein said measured screening marker levels from said first and second stages of pregnancy are highly correlated with one another.

24. (Cancelled)

25. (Cancelled)

26. (Previously presented) A method as claimed in claim 20 wherein said measured second screening marker levels from said first and second stages of pregnancy are highly correlated with one another.

27. (Previously presented) A method as claimed in claim 20 further comprising:

measuring at least one ultrasound screening marker from an ultrasound scan taken at one of said first and second stages of pregnancy; and

wherein determining determines said Down's risk estimate further using said ultrasound screening marker.

28-31. (Cancelled)

32. (Currently amended) A computer system for providing risk data representing a likelihood of a fetus carried by a pregnant mother having a chromosomal abnormality using a first biological parameter and a second biological parameter, both of which parameters are ~~being~~ suitable for screening said fetus for said chromosomal abnormality, the computer system comprising:

a data store operable to store data to be processed;

an instruction store storing processor implementable instructions; and

a processor coupled to said data store and to said instruction store and configured to load and implement said stored instructions, said instructions comprising instructions for controlling the processor to:

input first data from a first stage of pregnancy of said mother, said first data comprising data representing a first value of said first biological parameter which is PAPP-A, ~~said first biological parameter comprising one of total hCG, PAPP-A, Inhibin-A, AFP, and uE3,~~ and data representing a first value of a second biological parameter, said second biological parameter comprising one of total hCG, ~~PAPP-A,~~ Inhibin-A, AFP,

and uE_3, ~~wherein said second biological parameter is suitable for screening said fetus for said chromosomal abnormality~~;

input second data from a second, later stage of said pregnancy, said second data comprising data representing a second value of said first biological parameter and data representing a second value of a second biological parameter;

determine said risk data from said fast and second data by expressing each of said first and second data as a logarithm of a multiple median value by dividing each of said first and second data by a corresponding predicted median value to form a feature vector y;

~~determining~~ determine said likelihood ratio data from a ratio of a probability of an unaffected pregnancy given feature vector y and a probability of an affected pregnancy in which said fetus has said abnormality given feature vector y; and

output said determined risk data,

wherein said first biological parameter is a marker for said chromosomal abnormality at the first stage of pregnancy and has substantially no value as a marker during the second stage of pregnancy, and

wherein said second biological parameter is a marker for said chromosomal abnormality at said second stage of pregnancy and has substantially no value as a marker during the first stage of pregnancy.

33-39. (Cancelled).

40. (Previously presented) A method as claimed in claim 1, wherein in a cohort of pregnancies having said abnormality said first biological parameter is selected such that a correlation coefficient of said first and second values of said parameter is greater than 0.6.

41. (Previously presented) A method as claimed in claim 1, wherein in a cohort of pregnancies having said abnormality said second biological parameter is selected such that a correlation coefficient of said first and second values of said parameter is greater than 0.6.

42. (New) The method of claim 1 comprising a third biological parameter,

said first data comprising data representing a first value of said third biological parameter, said third biological parameter comprising one of total hCG, Inhibin-A, AFP, and uE_3, said third biological parameter being different than said second biological parameter; and

said second data comprising data representing a second value of said third biological parameter,

wherein said third biological parameter is a marker for said chromosomal abnormality at said second stage of pregnancy and has substantially no value as a marker during the first stage of pregnancy.

43. (New) The method of claim 20, comprising:

measuring a third biochemical screening marker level from said first stage of pregnancy by assaying a sample obtained from the pregnant woman at said first stage of pregnancy for said third biochemical screening marker, said third biochemical screening marker comprising one of total hCG, Inhibin-A, AFP, and uE_3, said third biochemical screening marker being different than said second biochemical screening marker; and

measuring a level of said third biochemical screening marker at said second stage of pregnancy by assaying a sample obtained from the pregnant woman at said second stage of pregnancy for said third biochemical screening marker;

wherein said third biochemical screening marker is a marker for said chromosomal abnormality at said second stage of pregnancy and has substantially no value as a marker during the first stage of pregnancy.

44. (New) The computer system of claim 32 comprising a third biological parameter,

said first data representing a first value of said third biological parameter, said third biological parameter comprising one of total hCG, Inhibin-A, AFP, and uE_3, said third biological parameter being different than said second biological parameter; and

said second data comprising data representing a second value of said third biological parameter,

wherein said third biological parameter is a marker for said chromosomal abnormality at said second stage of pregnancy and has substantially no value as a marker during the first stage of pregnancy.